

Anxiety, Depression and Quality of Life in Italian Youths with Type 1 Diabetes Mellitus

Silvana Zaffani, Isabella Maccagnan, Anita Morandi, Lara Comerlati, Alberto Sabbion, Giovanna Contreas, Marco Marigliano* and Claudio Maffei

Regional Center for Pediatric Diabetes, Pediatric Diabetes and Metabolic Disorders Unit, University of Verona, Verona, Italy

*Corresponding author: Marco Marigliano, MD, Regional Center for Pediatric Diabetes, Pediatric Diabetes and Metabolic Disorders Unit, Pad. 3, Ospedale Civile Maggiore, Piazzale Stefani, 1 - 37126 Verona, Italy, Tel: + 39 045 8127655; Fax: + 39 045 8127660; E-mail: marco.marigliano@univr.it

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Abstract

Background: Psychological problems and low quality of life (QoL) in children with type 1 Diabetes Mellitus (T1DM) were reported as correlated with T1DM. This study wants to test if the prevalence of anxiety and depression is higher in young patients with T1DM than in controls, if the level of QoL is lower and if anxiety and QoL correlate with glyco-metabolic control.

Methods: A total of 100 children with T1DM, aged 8-13 years, were recruited and 114 healthy children were recruited as controls. All children with T1DM were receiving a routine psychological support. Patients and controls underwent three questionnaires [the Self Administrated Psychiatric Scale Scales for Children and Adolescents (SAFA), the Children's Depression Inventory (CDI) and the Pediatric Quality of Life Inventory (PedsQL)]. Diabetes-related, physical and socio-demographic parameters were also collected.

Results: SAFA, CDI and PedsQL mean score were not statistically different in T1DM and in control group. Just the "separation anxiety" scale showed significantly higher mean score in the T1DM than in the control group (43.77 ± 10.34 vs. 23.11 ± 18.25 , $p < 0.01$). A significant correlation between QoL and metabolic control (HbA1c) ($r = 0.21$, $p < 0.05$) was found. HbA1c increased with the mother's education ($r = 0.42$, $p < 0.05$) and occupation level ($r = 0.35$, $p < 0.05$), and with the number of siblings ($r = 0.20$, $p < 0.05$).

Conclusions: T1DM is not a condition promoting per se more psychological discomfort even if a higher level of separation anxiety was shown. Interestingly, a higher level of self-perceived QoL was associated with worse glycometabolic control.

Significant findings of the study:

1. The anxiety, depression and QoL levels were not significantly different in children with T1DM vs healthy peers even if children with T1DM showed higher separation anxiety
2. There was not association between psychological parameters and the glycometabolic control (HbA1c)

What this study adds:

The self-perceived QoL, in subjects with T1DM, was higher in subjects with worse glycometabolic control and lower in patients with better glycometabolic control

Psycho-educational and therapeutic programs should sustain parents and children with T1DM

Keywords: Anxiety; Depression; Quality of life; Type 1 Diabetes Mellitus; Youth

Introduction

Diabetes is a lifelong disease that affects biological, social and psychological components. Children with type 1 Diabetes Mellitus (T1DM) live with daily stress and pressures by parents, clinicians and other caregivers. As reported in the Diabetes Control and Complication Trial [1], in order to achieve optimal metabolic control, children with diabetes have to cope on a daily basis with a complex,

intensive treatment regimen. The effort required for self-care and for adjustment to diabetes exposes children at risk of psychological difficulties and distress: the initial period and the first years after the diagnosis are characterized by psychological maladjustment with sadness, anxiety, withdrawal and dependency [2,3]. Afterwards, types and severity of the psychological/psychiatric effects of diabetes burden on children were described across different studies in literature, as extremely heterogeneous and changeable over time, with a reported increased risk for adolescents [4,5].

According to recent reports, the prevalence of anxiety and depression looks to be higher in children with T1DM than in healthy

peers [6-10]. Even if the evidence of a higher incidence of psychological disorders in adolescents with T1DM is well described, this is not so clear in younger children. Moreover, a recent meta-analysis supports the idea that children with T1DM show higher levels of depression, anxiety and psychological distress compared to healthy peers, but the differences are minimal and influenced by several factors, such as gender, time since diagnosis, etc [4-11].

Another psycho-social parameter, possible expression of psychological discomfort and life stress, is the Quality of Life (QoL), defined as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns [12]. Several studies reported that children and adolescents with T1DM experience a poorer QoL in comparison to healthy peers [13,14]. However, the link between T1DM and QoL is not consistent among studies and for some authors, children with T1DM may experience similar QoL to healthy children [15-17]. It would be important to clarify the relationship between diabetes and psychological-QoL aspects and trying to understand if psychological adjustments, due to T1DM management, could affect glycemic control and if adherence to self-management requires good QoL and psychological wellbeing.

Actually, this hypothesis is confirmed by several studies reporting that the presence of anxiety, depression and other emotional disorders in patients with T1DM are associated with poor glycemic control, with a higher risk of severe hypoglycemia and ketoacidosis (DKA) [18-22]. Similarly, in regards with QoL, some reports showed that a high QoL is associated with a good glycemic control [13,23-28]. On the other hand, other reports did not support those findings and failed to show any association between psychological status or well-being and HbA1c [11,14,29,30].

The aims of this study were: i. to measure the prevalence of anxiety, depression, and the level of QoL in a sample of Italian youths with T1DM; ii. to test the hypotheses that the prevalence of psychological disorders is higher in children with T1DM vs healthy controls; iii. to assess if the level of anxiety, depression, and QoL is associated with the level of the glyco-metabolic control (HbA1c).

Methods

Subjects

A total of 100 children with T1DM, aged 8-13 years, (males/females: 55/45) were recruited consecutively at the Regional Center for Pediatric Diabetes in Verona (Italy). All children with T1DM were receiving a routine psychological support; this was in accordance with the IDF/ISPAD International Guidelines [31]. A total of 114 healthy children, age- and sex- matched control subjects (males/females: 56/58, aged 8-13 years), living in the same geographical area, were recruited at primary and intermediate school.

Inclusion criteria were: T1DM; duration of diabetes for at least 12 months (just for children with diabetes); Caucasian ethnicity. Exclusion criteria were: chronic illnesses or chronic use of drugs, (except insulin for children with T1DM), treatment with continuous subcutaneous insulin infusion (CSII), other autoimmune disorders (thyroiditis, celiac disease). Children with T1DM who were included in the study were all following multiple dose injection treatment with four-five injections per day, one long-acting insulin and three-four regular or short-acting insulin before main meals. The study protocol was in accordance with the 1975 Declaration of Helsinki, revised in

2008, and approved by the Ethics Committee of the Local Health Care Unit (ULSS 20) of Verona. Informed consent was obtained from all the children and their parents.

Physical and socio-demographic parameters

Body weight was measured to the nearest 0.1 kg on standard physician's beam scales, with the child wearing only underwear and no shoes. Height was measured to the nearest 0.1 cm on standardized, wall-mounted height boards. The body mass index (BMI) was calculated as weight (kilograms) divided by height (meters) squared. The standard deviation score of the BMI (BMI z score) was also calculated. The same investigator measured height and weight. Pubertal development was clinically assessed by Tanner stages [32]. Diabetes-related variables [age at diagnosis, duration of disease, number of insulin injection, total daily insulin dose (U/kg), number of blood glucose measurements (BGM)] were collected and a blood sample was taken for HbA1c determination. HbA1c was measured using high-performance liquid chromatography with a Biorad variant 2 cation exchange column; the instrument was calibrated against Diabetes Control and Complication Trial (DCCT)-approved standards. Parental socio-demographic characteristics (marital status of parents, number of siblings, education and occupation levels) were collected. We categorized education levels in primary, secondary, high school, college or more and occupation levels in professional/executive, office worker/manager and unemployed/worker/housewife [33]. Parents of control subjects did not agree to give consent for collecting their socio-demographic and children's physical data.

Measures of psychological parameters and QoL

All the patients and controls underwent three questionnaires (for anxiety, depression and QoL measures), individually administered by the same psychologist.

Anxiety symptoms: Children completed the Self Administrated Psychiatric Scales for Children and Adolescents (SAFA), a validated Italian psychometric test to evaluate psychiatric condition in children and adolescents aged 8 to 18 [34]. SAFA includes a total of six scales, one of which for evaluation of anxiety (SAFA-A), with four subscales: generalized anxiety, meaning tension/uneasiness and apprehensiveness/preoccupations about the future; social anxiety, which investigates the characteristics of the avoidant disorder [DSM III R]; separation anxiety, which investigates separation, apprehension about loss and abandonment; school-related anxiety.

Depressive symptoms: Children completed the validated Italian version of the Children's Depression Inventory (CDI) [35]. The CDI, a self-report instrument, assesses depressive symptoms including disturbance in mood, self-evaluation, physical function, and interpersonal behaviors. It is validated in the age's range 8-17 years and consists of 27 items, with scores ranging from 0 to 54. Higher scores reflect greater symptomatology. The cut-off point for elevated levels of depressive symptoms is not universally agreed upon, we used the criterion score of 16 [14].

Quality of life: Generic QoL both of children with T1DM and healthy children was measured using PedsQLTM (Pediatric Quality of Life InventoryTM version 4.0), developed by Dr James W. Varni [36,37]. This standardized instrument consists of a core measure of global health-related quality of life (HRQoL), suitable for all the pediatric population, and supplemental illness-specific module. In this study we use the Generic Core Scales (physical functioning, emotional

functioning, social functioning, school functioning, psychosocial and total functioning) and the PedsQLTM Diabetes Module Scale containing 28 items distributed in scales (diabetes symptoms, treatment barriers and adherence, worry, communication and total diabetes). Items are reverse scored and linearly transformed to a 0-100 scale, with the higher scores indicating a better QoL. Total scale scores are computed as the mean across all items scored in that scale. The Italian version of PedsQL 4.0 demonstrates acceptable reliability and validity and it has been utilized by other authors [16].

Statistical analyses

Socio-demographic data are showed as median and IQI, whereas psychological rates are shown as means and standard deviation (SD). Comparisons of anxiety-depression-QoL scores between children with T1DM and controls were performed by Student's t test. Comparison between categorical data was done by χ^2 test. Pearson correlation coefficient was calculated to assess the level of relationship between variables. Multiple regression analysis was performed to explore the relation between dependent variables (CDI, SAFA and PedsQLtm scores) and anthropometric, metabolic and socio-demographic variables. A p value <0.05 was considered statistically significant. Data were processed using SPSS 19.0 for Windows.

Results

Physical and socio-demographic characteristics

Demographic, anthropometric and diabetes-related parameters of children with T1DM are shown in Table 1. Fifty-five children with T1DM were pre-pubertal and 45 were pubertal. Ninety-one (91%) children had both parents living together and nine (9%) had separated/divorced parents and live in a single parent family; the mean number of siblings was 0.96 (SD = 0.72).

	T1DM group (n=100)	
	median	IQI
Age (year)	11.4	9.5-12.6
Duration of diabetes (years)	4.33	1.66-6.8
Onset age	6.91	3.95-9
Weight (kg)	39.4	31.2-48.5
Height	148.5	135-157.5
BMI	17.9	16.5-19.9
BMI z scores	0.00	-1.32+1.02
HbA1c (%)	8	7.6-8.6
Insulin dose (U/day)	0.82	0.70-1
Blood Glucose Measurements/day	5	4-5

Table 1: Socio-demographic and physical characteristics of youths with T1DM: data are shown as median and IQI

49% of fathers and 45.5% of mothers had a medium-high level of occupation (managers, lawyers, executive director, teachers, business owners) 42.9% of fathers and 15.2% of mothers were generic workers

(unskilled, semi-skilled or skilled, merchants, minor business owners) and 38.4% housewives. Comparison between children with T1DM and controls did not show any significant difference in gender distribution (M/F 55/45 vs 56/58, $\chi^2= 0.88$, p=NS) and age (11.1 ± 1.83 yrs vs. 10.68 ± 1.79 yrs, p=NS).

Psychological scores and correlations

Questionnaires were completely filled out by all children. The mean scores of SAFA, CDI, PedsQLtm questionnaire are shown in Table 2.

	T1DM group	Control Group	p value
SAFA			
Generalized Anxiety	48.23 (9.94)	48.71 (9.77)	NS
Social Anxiety	49.61 (9.41)	48.41 (9.27)	NS
Separation Anxiety	43.77 (10.34)	23.11 (18.25)	0.001
Scholastic Anxiety	45.81(9.19)	47.93 (10.34)	NS
Total Score	46.17 (9.90)	46.76 (9.35)	NS
CDI			
	7.06 (4.97)	7.04 (5.4)	NS
PEDS-QoL Generic Core Scale child self-report			
Total Score	77.82 (12.64)	78.48 (11.54)	NS
Physical Health	80.59 (12.22)	78.67 (12.76)	NS
Psychosocial Health	76.47 (13.94)	78.40 (13.42)	NS
PEDS-QL Diabetes Module Total Score	76.41 (13.01)	--	--

Table 2: Depression, anxiety and QoL scores (mean and SD) in T1DM and control group. Data are shown as mean and standard deviation (SD)

Anxiety symptoms

An abnormal anxious status (SAFA total score \geq 70th percentile) was found in one child with T1DM (1%) and in three control children (2.6%). The scores of all the other subjects were in the normal range. Just one SAFA subscale, "separation anxiety", showed significantly ($p < 0.01$) higher mean score in the T1DM group than in control group (43.77 ± 10.34 vs. 23.11 ± 18.25). In the formed group, separation anxiety score was significantly higher in pre-pubertal than in pubertal children (45.7 ± 11.3 vs. 41.5 ± 8.6 , $p < 0.05$). In both groups, social anxiety was significantly correlated with age: children with T1DM $r=0.23$, $p < 0.03$; control children: $r=0.26$, $p < 0.01$.

Depression

Median CDI score were within the normal range (CDI < 16) in both T1DM and control children, although 7 children with T1DM (7%) and 9 controls (8%) showed pathological CDI values. The distribution of subjects with positive score for depression was not significantly different in the two groups ($\chi^2 = 0.05$, p=NS). However, in children with T1DM, the positive score for depression was found in 6 pre-pubertal children and in 1 pubertal child. On the contrary, in control children, the positive score for depression was found in 1 pre-pubertal

child and in 7 pubertal children ($\chi^2 = 0.2$, $p < 0.05$). No gender effect was found ($\chi^2 = 1.54$, $p = \text{NS}$).

Parents' socio-demographic characteristics were not associated with depression score in their children with T1DM.

Quality of Life (QoL)

Children with T1DM showed general QoL (general module) mean score not statistically different from that of controls (77.8 ± 12.6 vs. 78.5 ± 11.5 , $p = \text{NS}$). In T1DM group, at the diabetes-specific module, QoL was over the mean value in the medium-high range (mean=76.4, SD=13.0). Significant correlations between general QoL and psychopathological symptoms (anxiety and depression total scores) were found in children with T1DM ($r = -0.61$, $p < 0.001$; $r = -0.52$, $p < 0.001$, respectively) and in controls ($r = -0.45$, $p < 0.001$; $r = -0.52$, $p < 0.001$, respectively). In particular, in both groups, the depression score was negatively correlated with perceived physical health QoL (T1DM: $r = -0.24$, $p < 0.05$; controls: $r = -0.36$, $p < 0.001$) and psychosocial health QoL (T1DM: $r = -0.55$, $p < 0.001$; controls: $r = -0.56$, $p < 0.001$).

Psychological status and HbA1c

A significant correlation between psycho-social QoL and HbA1c levels ($r = 0.21$, $p < 0.05$) was found. No other significant correlations between psychological indices (anxiety, depression and QoL) and HbA1c were found (data not showed).

Family structure/socio-demographic factors and HbA1c

HbA1c increased with the mother's education ($r = 0.42$, $p < 0.05$) and occupation level ($r = 0.35$, $p < 0.05$), and with the number of siblings ($r = 0.20$, $p < 0.05$). Father's education and occupation level were not associated with HbA1c. Father's education level was significantly associated with general QoL ($r = 0.38$, $p < 0.05$) and psychosocial QoL ($r = 0.33$, $p < 0.05$), whereas mother's was not. No significant association was found with parents' occupational level.

Discussion

The main findings of this study are three: i. the anxiety, depression and QoL levels were not significantly different in children with T1DM vs healthy peers even if children with T1DM showed higher separation anxiety; ii. there was not association between psychological parameters and the glycometabolic control (HbA1c); iii. the self-perceived QoL, in subjects with T1DM, was higher in subjects with worse glycometabolic control and lower in patients with better glycometabolic control. Our data shows that the diagnosis of diabetes per se is not enough to increase the incidence of psychological disorders, although diagnosis may be followed by an increased initial risk of dysphoria, sadness, withdrawal and dependency in youths [4].

Although no difference in overall psychological adjustment were found in the two groups, children with T1DM showed higher separation anxiety than healthy children: in particular, the younger children reported more difficulties in autonomy from parents. It is possible that the parents of young children with T1DM are more vulnerable in the relationship with them than with healthy peers. These parents may be oversensitive to the physical, social or emotive problems of their children and they generally underestimate their children's QoL, like in other chronic illness [38-40]. As a consequence, parents tend to over-support for long-time their children.

Depression scores were not different in the two groups, although, in children with T1DM, an age effect is detectable. In particular, according to literature, older control children had a higher chance to show depressive condition than younger ones. On the contrary, children with T1DM showed an opposite trend: depressive scores were significantly more common in younger than in the older children. The potential reason why older children with diabetes have a lower chance to be depressed than younger ones may be the level of autonomy and consciousness of personal resources in diabetes management, which is higher in adolescence. This hypothesis seems to find indirect support from the evidence that separation anxiety is high in these children, suggesting an increased need of support from parents.

As regards QoL, both groups showed good QoL levels and children with diabetes perceived their life as satisfactory and they felt confident in their abilities to manage diabetes, with relatively low worries about the illness. This finding support what previously reported by others [15,16]. As expected, anxious and depressive symptoms were negatively correlated with the QoL.

As regards gender, the "female vulnerability" to psychological distress and lower QoL was not confirmed in this study [13,14,24,25]. A potential explanation is the younger age of the children participating in this study than in the previous ones. It is likely that in the pre-adolescents the gender variable is not decisive.

We have not found any association between anxiety/depressive symptoms and metabolic control. Interestingly, however a poorer psychosocial QoL was correlated with lower values of HbA1c: probably, children with good compliance at the diabetes' requests and at the daily practices live with more diabetes-specific limitations, in and out of the family.

Furthermore, we highlighted a correlation between HbA1c and socio-demographic family's aspects. In our population, the mother's higher education level and occupational level or living in a family with a high number of siblings, were associated with the worsening of HbA1c. As reported in the DAWN YOUTH Survey the Italian way for taking care of T1DM is parent-oriented [41]. This could probably explain why we found a correlation between family structure and metabolic control. As it was shown, the parental over-involvement is an important determinant of decreased metabolic control in adolescent [42].

This study has potential limitation: i. the lack of a control group of not-psychologically supported children with T1DM. The IDF/ISPAD International Guidelines underlines the importance of the assessment of the psychosocial functioning in the overall evaluation of the care of young people with T1DM. Therefore, all pediatric centers should assure psychological support to patients and their families. On this basis, it is considered to be unethical to offer psychological support only to a sub-group of patients with T1DM; ii. all patients were recruited from a single pediatric unit, where psychological care is provided to each patient and family with regularity, two or more times per year, since the diabetes onset. A psychologist, specialized in care of children with T1DM, gives the support needed to children and their family, in particular in developing emotional strategies to cope with a lifetime disease as T1DM. This regular screening and the early intervention may improve psychosocial adjustment and may increase well-being. Therefore, it is possible that patients and their families that may not receive this kind of psychological support may have a higher incidence of psychological difficulties and distress; iii. we did not involve the parents in the research and we did not assess family

dynamics and variables, such as cohesion and conflict, influencing the well-being. Many studies reported that parents showed a worse generic and diabetes-related QoL and the parental diabetes-related stress influenced the children adaptation to disease and glycemic control [13,14].

The strengths of this study were as follows: i. the novelty: the novelty of the study, not previously conducted on a Southern European pediatric population, where families are characterized by different dynamics and attitudes towards Northern European population; ii. the study design: the simultaneous evaluation of the levels of anxiety, depression, and QoL in a group of youths with T1DM.

Conclusion

In conclusion, anxiety, depression and QoL levels were not significantly different in children with T1DM, treated with a multi-disciplinary approach accordance with IDF/ISPAD guidelines, and in healthy children; this suggests that T1DM is not a condition promoting per se more psychological discomfort than in healthy peers and did not affect the psychological status in a group of children aged 8-13 years old. At the same time, children with T1DM showed a higher level of separation anxiety; in particular, the younger children with T1DM reported more difficulties in autonomy from parents that tend to over-support for long-time them. Interestingly, the self-perceived QoL was inversely associated with the glycometabolic control suggesting that further work has to be done to improve the relationship between QoL and glycometabolic control.

The results of this study suggest that psycho-educational and therapeutic patient education programs related to children with T1DM and their families, should sustain parents in the task of balancing emotional and practical support provided to the child. This should be done with the aim to improve their empowerment and autonomy in the management of T1DM.

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